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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/076,404	05/12/1998	DAVID J. ECKER	IBIS-0007US	4802

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EXAMINER	
BRUSCA, JOHN S	
ART UNIT	PAPER NUMBER
1631	
MAIL DATE	DELIVERY MODE
11/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/076,404	ECKER ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,26,30,32-35,37,38,40,41,43,44,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are pending.

Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are rejected.

Specification

2. The objection to the specification in the Office action mailed 07 February 2008 is withdrawn in view of the amendment to the specification filed 06 August 2008.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing includes the following considerations:

a) The specification does not reduce to practice an embodiment of the claimed subject matter, which requires analysis of a human target RNA comprising a molecular interaction site that is less than 30 nucleotides in length.

b) The specification does not disclose a structure of a human target RNS comprising a molecular interaction site that is less than 30 nucleotides in length. The specification shows example 1 on page 131 that states that human IRE comprises a protein binding site of approximately 30 nucleotides instead of the claimed limitation of less than 30 nucleotides.

c) The specification does not provide identifying characteristics such as structure, physical characteristics, or a known correlation between the claimed functional characteristic and structure of human target RNA that comprises a molecular interaction site that is less than 30 nucleotides in length.

d) The method of using the claimed subject matter requires obtaining the structure of human target RNA that comprises a molecular interaction site that is less than 30 nucleotides in length.

e) The level of skill in the field of molecular biology is high.

f) The specification does not establish that there is any predictability in correlating the claimed function and the structure of human target RNA that comprises a molecular interaction site that is less than 30 nucleotides in length.

The specification describes a human target RNA termed the iron response element (IRE) element on page 131, example 1. The specification on page 131 characterizes the IRE element as "The IRE is an RNA element of approximately 30 nucleotides that folds into a hairpin structure and binds a specific protein." The specification does not describe the structure of human target RNA sequences with an interaction site that is **less** than 30 nucleotides in length. The specification does not describe any species of the claimed genus of human molecular interaction

sites in sufficient detail to establish that the applicants had possession of the claimed subject matter at the time of filing.

5. Applicant's arguments filed 06 August 2008 have been fully considered but they are not persuasive. The applicants note that the claim requires that the molecular interaction site is less than 30 nucleotides rather than requiring a human target RNA that is less than 30 nucleotides. It is the understanding of the Office that while the claimed human target RNA may be considerably larger than the molecular interaction site it comprises, the claimed subject matter requires that the molecular interaction site within the human target RNA is less than 30 nucleotides in length. The applicants point to recitation of "less than 30 nucleotides" on page 16, line 1, however the recitation does not serve to describe a representative number of species of the claimed genus of human molecular interaction sites. Because the specification does not describe any species of the claimed genus of human target RNA comprising a molecular interaction site of less than 30 nucleotides the rejection is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al. in view of Arenas et al. in view of Sezerman et al. in view of Greig et al. in view of Hentze et al.

The claims are drawn to a method of using an in silico virtual library of compound structure data to identify a structure that binds a human target RNA with an interaction site of less than 30 nucleotides. The compounds are synthesized and analyzed by generation of ionized fragments (exemplified in the specification by use of mass spectroscopy) of the RNA complexed with the compound. In some embodiments the identified compounds are ranked for binding strength, the target RNA is compared to RNA of different taxonomic species, and the target has a stem, hairpin, or loop structure that is within an untranslated region.

Murray et al. shows a method of designing and use of virtual libraries of compounds to select structures that have a desired binding specificity in the abstract and throughout. Murray et al. shows ranking of members of the library on pages 203-204 for predicted binding strength. Murray et al. shows the general applicability of their method throughout and shows an example of thrombin inhibitors, and their subsequent synthesis and testing on page 204. Murray et al. does not show RNA binding compounds.

Arenas et al. shows a screening method for compounds that bind RNA in the abstract and throughout. Arenas et al. shows that the compounds may be selected from peptides or small organic molecules in column 5, lines 62-67, and antibiotics in column 1, lines 56-59. Arenas et

al. shows in column 1 that small molecules can be used to block functions of the target RNA. Arenas et al. shows in column 6, lines 40-41 that the target RNA may be from any living organism.

Sezerman et al. shows in the abstract and throughout methods of using virtual peptide structures to measure binding affinity to a binding target.

Greig et al. shows use of electrospray mass spectroscopy of peptide-oligonucleotide complexes to measure binding strength, with results shown in figure 2.

Hentze et al. shows a human iron responsive element (IRE) in the 5' untranslated portion of ferritin H chain messenger RNA (mRNA). Hentze et al. shows in figure 1, and Table 1 that the element confers responsiveness to media iron content to increase translation of the mRNA. Hentze et al. show in Figures 2 and 3 construction and assay of a 26 base synthetic oligonucleotide fragment of the IRE. Hentze et al. compares the human sequence to orthologous sequences from other species in figure 2 and the discussion on page 1572 and concludes that the sequence is highly conserved during evolution. Hentze et al. shows in Figure 3 that the fragment of the IRE is sufficient to confer iron responsiveness of translation to a human growth hormone reporter gene.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening method of Murray et al. by use of the RNA targets of Arenas et al. because Arenas et al. shows bioassays that screen for compounds that bind to RNA targets. It would have been further obvious to use mass spectroscopy to analyze binding strength because Sezerman shows that peptides may be analyzed in silico for binding, and Greig et al. shows that mass spectroscopy may be used to determine the binding affinity of a complex

of a peptide and an oligonucleotide, and experimental determination of binding strength is an important parameter for determination of biological activity. It would have been further obvious to use the IRE target sequence of Hentze et al. because Hentze et al. shows that the human IRE RNA target sequence has a role in cell iron metabolism, and further can be used to confer regulation of translation on a mRNA of choice. Development of compounds that bind to the human IRE would allow for development of compounds that inhibit or enhance expression of wild type or recombinant genes in human cells as suggested by Arenas to allow for insights into the function of naturally occurring mRNA or to regulate gene expression of recombinant genes comprising the IRE.

9. Applicant's arguments filed 06 August 2008 have been fully considered but they are not persuasive. The applicants state that the applied references do not show comparison of a target RNA to nucleotide sequences of different taxonomic species, however Hentze et al. shows that comparison as noted in the revised rejection above. The applicants state that there is no motivation to contact the target RNA with a binding compound and to further study the resulting complex by mass spectrometry. However such motivation is discussed in the rejection above, particularly with regard to the Greig et al. reference. The applicants state that the Murray et al. reference shows in silico analysis which is incompatible with the mass spectrometry analysis of Greig et al., however the in silico and experimental approaches of these two references are not in conflict, the two references show complementary methods of studying formation of binding complexes, each with advantages such as speed and ability to assay a large range of potential compounds for the in silico method, and accuracy and experimental confirmation of predicted complex formation for the mass spectrometry method.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/
Primary Examiner
Art Unit 1631

jsb
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